



1 GAATTCCCAA AGACAAAatg gatttttcaag tgcagatttt cagcttcctg
51 ctaatcagtg cctcagtcac aatatccaga ggacaaattg ttctcaccac
101 gtctccagca atcatgtctg catctccagg ggagaagggtc accatgacct
151 gcagtgccag ctcaagtgtg agttacatga actgggtacca gcagaagtca
201 ggcacctccc ccaaaagatg gatttatgac acatccaaac tggcttctgg
251 agtccctgct cacttcaggg gcagtgggtc tgggacctct tactctctca
301 caatcagcgg catggaggct gaagatgctg ccacttatta ctgccagcag
351 tggagtagta accattcac gttcggctcg gggacaaagt tggaaataaa
401 ccgggctgat actgcaccaa ctgtatccat cttcccacca tccagtgagc
451 agttaacatc tggagggtgcc tcagtcgtgt gcttcttgaa caacttctac
501 cccaaagaca tcaatgtcaa gtggaagatt gatggcagtg aacgacaaaa
551 tggcgtcctg aacagttgga ctgatcagga cagcaaagac agcacctaca
601 gcatgagcag caccctcacg ttgaccaagg acgagtatga acgacataac
651 agctataacct gtgaggccac tcacaagaca tcaacttcac ccattgtcaa
701 gagcttcaac aggaatgagt gtTAGAGACA AAGGTCCTGA GACGCCACCA
751 CCAGCTCCCA GCTCCATCCT ATCTTCCCTT CTAAGGTCTT GGAGGCTTCC
801 CCACAAGCGC tTACCACTGT TGCGGTGCTC TAAACCTCCT CCCACCTCCT
851 TCTCCTCCTC CTCCCTTTCC TTGGCTTTTA TCATGCTAAT ATTTGCAGAA
901 AATATTCAAT AAAGTGAGTC TTTGCCTTGA AAAAAAAAAA AAA
(SEQ ID NO:4)

FIG. 1a

1 MDFQVQIFSF LLISASVIIS RGOQIVLTQSP AIMSASPGEK VTMTCSASSS
51 VSYMNWYQQK SGTSPKRWIY DTSKLASGVP AHFRGSGSGT SYSLTISGME
101 AEDAATYYCQ QWSSNPFTFG SGTKLEINRA DTAPTVSIFP PSSEQLTSGG
151 ASVVCFLNNF YPKDINVKWK IDGSERQNGV LNSWTDQDSK DSTYSMSSTL
201 TLTKDEYERH NSYTCEATHK TSTSPIVKSF NRNEC* (SEQ ID NO:5)

FIG. 1b

11/11/11

1	GAATTCCCCT	CTCCACAGAC	ACTGAAAAC	CTGACTCAAC	ATGGAAAGGC
51	ACTGGATCTT	TCTACTCCTG	TTGTCAGTAA	CTGCAGGTGT	CCACTCCCAG
101	GTCCAGCTGC	AGCAGTCTGG	GGCTGAACTG	GCAAGACCTG	GGGCCTCAGT
151	GAAGATGTCC	TGCAAGGCTT	CTGGCTACAC	CTTTACTAGG	TACACGATGC
201	ACTGGGTAAA	ACAGAGGCCT	GGACAGGGTC	TGGAATGGAT	TGGATACATT
251	ATTCCTAGCC	GTGGTTATAC	TAATTACAAT	CAGAAGTTCA	AGGACAAGGC
301	CACATTGACT	ACAGACAAAT	CCTCCAGCAC	AGCCTACATG	CAACTGAGCA
351	GCCTGACATC	TGAGGACTCT	GCAGTCTATT	ACTGTGCAAG	ATATTATGAT
401	GATCATTACT	GCCTTGACTA	CTGGGGCCAA	GGCACCCTC	TCACAGTCTC
451	CTCAGCCAAA	ACAACAGCCC	CATCGGTCTA	TCCACTGGCC	CCTGTGTGTG
501	GAGATACAAC	TGGCTCCTCG	GTGACTCTAG	GATGCCTGGT	CAAGGGTTAT
551	TTCCCTGAGC	CAGTGACCTT	GACCTGGAAC	TCTGGATCCC	TGTCCAGTGG
601	TGTGCACACC	TTCCCAGCTG	TCCTGCAGTC	TGACCTCTAC	ACCCTCAGCA
651	GCTCAGTGAC	TGTAACCTCG	AGCACCTGGC	CCAGCCAGTC	CATCACCTGC
701	AATGTGGCCC	ACCCGGCAAG	CAGCACCAAG	GTGGACAAGA	AAATTGAGCC
801	ACCTCTTGGG	TGGACCATCC	GTCTTCATCT	TCCCTCCAAA	GATCAAGGAT
851	GTACTCATGA	TCTCCCTGAG	CCCCATAGTC	ACATGTGTGG	TGGTGGATGT
901	GAGCGAGGAT	GACCCAGATG	TCCAGATCAG	CTGGTTTGTG	AACAACGTGG
951	AAGTACACAC	AGCTCAGACA	CAAACCCATA	GAGAGGATTA	CAACAGTACT
1001	CTCCGGGTGG	TCAGTGCCCT	CCCCATCCAG	CACCAGGACT	GGATGAGTGG
1051	CAAGGAGTTC	AAATGCAAGG	TCAACAACAA	AGACCTCCCA	GCGCCCATCG
1101	AGAGAACCAT	CTCAAAACCC	AAAGGGTCAG	TAAGAGCTCC	ACAGGTATAT
1151	GTCTTGCCCTC	CACCAGAAGA	AGAGATGACT	AAGAAACAGG	TCACTCTGAC
1201	CTGCATGGTC	ACAGACTTCA	TGCCTGAAGA	CATTTACGTG	GAGTGGACCA
1251	ACAACGGGAA	AACAGAGCTA	AACTACAAGA	ACACTGAACC	AGTCCTGGAC
1301	TCTGATGGTT	CTTACTTTCAT	GTACAGCAAG	CTGAGAGTGG	AAAAGAAGAA
1351	CTGGGTGGAA	AGAAATAGCT	ACTCCTGTTT	AGTGGTCCAC	GAGGGTCTGC
1401	ACAATCACCA	CACGACTAAG	AGCTTCTCCC	GGACTCCGGG	TAAATGAGCT
1451	CAGCACCCAC	AAAACCTCTCA	GGTCCAAAGA	GAGACCCACA	CTCATCTCCA
1501	TGCTTCCCTT	GTATAAATAA	AGCACCCAGC	AATGCCTGGG	ACCATGTAAA
1551	AAAAAAAAAA	AAAGGAATTC	(SEQ ID NO:6)		

FIG. 2a

DKT 3 HEAVY CHAIN PROTEIN SEQUENCE DEDUCED FROM DNA SEQUENCE

1	<u>MERHWIFLLL</u>	<u>LSVTAGVHSQ</u>	VQLQQSGAEL	ARPGASVKMS	CKASGYTFTR
51	YTMHWVKQRP	GQGLEWIGYI	NPSRGYTNYN	QKFKDKATLT	TDKSSSTAYM
101	QLSSLTSEDS	AVYYCARYYD	DHYCLDYWGQ	GTTLTVSSAK	TTAPSVYPLA
151	PVCGDTTGSS	VTLGCLVKGY	FPEPVTLTWN	SGSLSSGVHT	FPAVLQSDLY
201	TLSSSVTVTS	STWPSQSITC	NVAHPASSTK	VDKKIEPRGP	TIKPCPPCKC
251	PAPNLLGGPS	VFIFPPKIKD	VLMSLSPIV	TCVVVDVSED	DPDVQISWFV
301	NNVEVHTAQT	QTHREDYNST	LRVVSALPIQ	HQDWMSGKEF	KCKVNNKDLP
351	APIERTISKP	KGSVRAPQVY	VLPPPEEEMT	KKQVTLTCMV	TDFMPEDIYV
401	EWTNNGKTEL	NYKNTEPVLD	SDGSYFMYSK	LRVEKKNWVE	RNSYSCSVVH
451	EGLHNHHTTK	SFSRTPGK*	(SEQ ID NO: 7)		

FIG. 2b

	1		23		42
	NN	N	N	N	N
RES TYPE	SBspSPESsSSbSsSSsPSPSPsPSsse*s*p*Pi^ISsSe				
0kt3vl	QIVLTQSPA ^I MSASPGEKVTMTCSASS.SVSYM ^N WYQQKSGT				
REI	DIQMTQSPSSLSASVGDRVTITCQASQDI ^I KYLNWYQQI ^T PGK				
	?	?			
	CDR1	(LOOP)	*****		
	CDR1	(KABAT)	*****		
		56			85
	N	NN			
RES TYPE	*IsiPpIeesesssSBEsePsPSBSSEsPspPsseesSPePb				
0kt3vl	SPKRWIYDTSKLASGVPAHFRGSGSGT ^S YSLTISGMEADAAT				
REI	APKLLIYEASN ^L QAGVPSRFSGSGSGTDYTET ^I SSLQPEDIAT (SEQ				
ID NO:8)					
	?	??		?	?
	***** CDR2 (LOOP/KABAT)				
			102	108	
RES TYPE	PiPIPIes**iPIIsPPSPSPSS				
0kt3vl	YYCQQWSSNPFTFGSGTKLEINR (SEQ ID NO:29)				
REIvl	YYCQQYQSLPYTFGQGTKLQIIR (SEQ ID NO:9)				
			?	?	
	*****		CDR3 (LOOP)		
	*****		CRD3(KABAT)		

FIG. 3

	NN N	23 26	32 35	N39	43	
RES TYPE	SESPs^SBssS^sSSsSpSpSPsPSEbSBssBePi^PIpiesss					
Dkt3h	QVQLQQSGAELARPGASVKMSCKASGYTFTRYTMNHWWKQRPGQ					
KOL	QVQLVESGGGVVQPGRSLRLSCSSSGFIFSSYAMYWVRQAPGK					
	?	??				
			*****	CDR1	(LOOP)	
			*****	CDR1	(KABAT)	

		52a	60	65	N N N	82abc	89
RES TYPE	IleIppp^ssssssss^ps^pSSsbSpseSsSseSp^pSpsSBssS^ePb						
Dkt3vh	GLEWIGYINPSRGYTNTNQKFKRKATLTTDKSSSTAYMQLSSLTSEDSAV						
KOL	GLEWVAIIWDDGSDQHYADSVKGRFTISRDN SKNTLFLQMDSLPPEDTGV						
	??			?? ?	?		?
	*****			CDR2	(LOOP)		
	*****			CDR2	(KABAT)		

	92 N	107	113	
RES TYPE	PIPIEissssiisssbibibi*EIPIP*spSBSS			
Dkt3vh	YYCARYYDDHY.....CLDYWGQGTTTLTVSS	(SEQ ID NO:30)		
KOL	YFCARDGGHGFCSSASCFGPDYWGQGTPTVTVSS	(SEQ ID NO:10)		
	*****	CRD4	(KABAT/LOOP)	

FIG. 4

DKT 3 HEAVY CHAIN CDR GRAFTS

1. gh341 and derivatives

	1	23	35	39	43	
Dkt3vh	QVQLQQSGAELARPGASVKMSCKASGYTFTRYTMHWVKQRPGQ					
gh341	QVQLVESGGGVVQDGRSLRLSCSSSGYTFTRYTMHWVRQAPGK					JA178
gh341A	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWVRQAPGK					JA185
gh341E	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWVRQAPGK					JA198
gh341*	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWVRQAPGK					JA207
gh341*	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWVRQAPGK					JA209
gh341D	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWVRQAPGK					JA197
gh341*	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWVRQAPGK					JA199
gh341C	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWVRQAPGK					JA184
gh341*	QVQLVQSGGGVVQPGRSLRLSCSASGYTFTRYTMHWVRQAPGK					JA203
gh341*	QVQLVESGGGVVQPGRSLRLSCSASGYTFTRYTMHWVRQAPGK					JA205
gh341B	QVQLVESGGGVVQPGRSLRLSCSSSGYTFTRYTMHWVRQAPGK					JA183
gh341*	QVQLVQSGGGVVQPGRSLRLSCSASGYTFTRYTMHWVRQAPGK					JA204
gh341*	QVQLVESGGGVVQPGRSLRLSCSASGYTFTRYTMHWVRQAPGK					JA206
gh341*	QVQLVQSGGGVVQPGRSLRLSCSASGYTFTRYTMHWVRQAPGK					JA208
KDL	QVQLVESGGGVVQPGRSLRLSCSSSGFIFSSYAMYWVRQAPGK					

FIG. 5a

	44	50	65	83	
Dkt3vh	GLEWIGYINPSRGYTNYNQKF K D K ATLT T D K SSSTAYMQLSSLT				
gH341	GLEWVAYINPSRGYTNYNQKF K D R FTIS R D N SKNTLFLQMDSL R				JA178
gH341A	GLEWIGYINPSRGYTNYNQKV K D R FTIS T D K SK S T A FLQMDSL R				JA185
gH341E	GLEWIGYINPSRGYTNYNQKV K D R FTIS T D K SK S T A FLQMDSL R				JA198
gH341*	GLEWIGYINPSRGYTNYNQKV K D R FTIS T D K SK N T A FLQMDSL R				JA207
gH341*	GLEWIGYINPSRGYTNYNQKV K D R FTIS R D N SKNT A FLQMDSL R				JA209
gH341D	GLEWIGYINPSRGYTNYNQKV K D R FTIS T D K SKNTLFLQMDSL R				JA197
gH341*	GLEWIGYINPSRGYTNYNQKV K D R FTIS R D N SKNTLFLQMDSL R				JA199
gH341C	GLEWVAYINPSRGYTNYNQKF K D R FTIS R D N SKNTLFLQMDSL R				JA184
gH341*	GLEWIGYINPSRGYTNYNQKV K D R FTIS T D K SK S T A FLQMDSL R				JA207
gH341*	GLEWIGYINPSRGYTNYNQKV K D R FTIS T D K SK S T A FLQMDSL R				JA205
gH341B	GLEWIGYINPSRGYTNYNQKV K D R FTIS T D K SK S T A FLQMDSL R				JA183
gH341*	GLEWIGYINPSRGYTNYNQKV K D R FTIS T D K SK S T A FLQMDSL R				JA204
gH341*	GLEWIGYINPSRGYTNYNQKV K D R FTIS T D K SK S T A FLQMDSL R				JA206
gH341*	GLEWIGYINPSRGYTNYNQKV K D R FTIS T D K SK N T A FLQMDSL R				JA208
KOL	GLEWVAIIWDDGSDQHYADSVKGRFTIS R D N SKNTLFLQMDSL R				

FIG. 5b

	84	95	102	113		SEQ ID NO:
Dkt3vh	SEDS	AVYYCARYYDDHY	CL	DYWGQGTTLTVSS		30
gH341	PEDT	GVYFCARYYDDHY	CL	DYWGQGTTLTVSS	JA178	30 11
gH341A	PEDT	<u>AVYYCARYYDDHY</u>	CL	DYWGQGTTLTVSS	JA185	12
gH341E	PEDT	GVYFCARYYDDHY	CL	DYWGQGTTLTVSS	JA198	13
gH341*	PEDT	GVYFCARYYDDHY	CL	DYWGQGTTLTVSS	JA207	14
gH341D	PEDT	GVYFCARYYDDHY	CL	DYWGQGTTLTVSS	JA197	15
gH341*	PEDT	GVYFCARYYDDHY	CL	DYWGQGTTLTVSS	JA209	16
gH341*	PEDT	GVYFCARYYDDHY	CL	DYWGQGTTLTVSS	JA199	17
gH341C	PEDT	GVYFCARYYDDHY	CL	DYWGQGTTLTVSS	JA184	18
gH341*	PEDT	<u>AVYYCARYYDDHY</u>	CL	DYWGQGTTLTVSS	JA203	19
gH341*	PEDT	<u>AVYYCARYYDDHY</u>	CL	DYWGQGTTLTVSS	JA205	20
gH341B	PEDT	<u>AVYYCARYYDDHY</u>	CL	DYWGQGTTLTVSS	JA183	21
gH341*	PEDT	<u>GVYFCARYYDDHY</u>	CL	DYWGQGTTLTVSS	JA204	22
gH341*	PEDT	GVYFCARYYDDHY	CL	DYWGQGTTLTVSS	JA206	23
gH341*	PEDT	GVYFCARYYDDHY	CL	DYWGQGTTLTVSS	JA208	24
KOL	PEDT	GVYFCARDGGHGF	CSSASCFGP	DYWGQGTPVTVSS		

FIG. 5c

DKT3 LIGHT CHAIN CDR GRAFTING

1. gL221 and derivatives

	1	24	34	42	
Dkt3vl	QIVLTQSPA	MSASPGEKVTMTCSASS.	SVSYMNWY	QQKSGT	
gL221	DIQMTQSPSSLSASVGDRVTITC	<u>SASS.</u>	<u>SVSYMNWY</u>	QQTPGK	
gL221A	<u>QIVMTQSPSSLSASVGDRVTITC</u>	<u>SASS.</u>	<u>SVSYMNWY</u>	QQTPGK	
gL221B	<u>QIVMTQSPSSLSASVGDRVTITC</u>	<u>SASS.</u>	<u>SVSYMNWY</u>	QQTPGK	
gL221C	<u>DIQMTQSPSSLSASVGDRVTITC</u>	<u>SASS.</u>	<u>SVSYMNWY</u>	QQTPGK	
REI	DIQMTQSPSSLSASVGDRVTITC	QASQDI	IKYLNWY	QQTPGK	
	43	50	56	85	
Dkt3vl	SPKRWIYDTSKLASGVPAHFRGSGSGT	SYSLTISG	MEAEDAAT		
gL221	APKLLIYDTSKLASGVPSRFSGSGSGT	DYFTISS	LQPEDIA	T	
gL221A	APKRWIYDTSKLASGVPSRFSGSGSGT	DYFTISS	LQPEDIA	T	
gL221B	APKRWIYDTSKLASGVPSRFSGSGSGT	DYFTISS	LQPEDIA	T	
gL221C	APKRWIYDTSKLASGVPSRFSGSGSGT	DYFTISS	LQPEDIA	T	
REI	APKLLIYEASNLQAGVPSRFSGSGSGT	DYFTISS	LQPEDIA	T	(SEQ ID NO:8)
	86	91	96	108	
Dkt3vl	YYCQQWSSNPFTFGSGTKLEINR				(SEQ ID NO:29)
gL221	YYCQQWSSNPETFGQGTKLQITR				(SEQ ID NO:25)
gL221A	YYCQQWSSNPETFGQGTKLQITR				(SEQ ID NO:26)
gL221B	YYCQQWSSNPETFGQGTKLQITR				(SEQ ID NO:27)
gL221C	YYCQQWSSNPETFGQGTKLQITR				(SEQ ID NO:28)
REI	YYCQQYQSLPYTEGQGTKLQITR				(SEQ ID NO:9)

CDR'S ARE UNDERLINED

FRAMEWORK RESIDUES INCLUDED IN THE GENE ARE DOUBLE UNDERLINED

FIG. 6